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BRAIN TUMORS; A STUDY OF CLINICAL AND POST-MORTEM RECORDS BEARING ON THEIR OPERABILITY AND THEIR SYMPTOMATOLOGY.[1]

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Statistics dividing autopsied cases of brain tumor into operable and inoperable allow the personal equation of the collector so great a range that uniformity of results can hardly be expected. The estimates of the writers who have studied the subject from this point of view vary materially. The average estimate of the various collectors as tabulated by Knapp[2] in 1899 was about 11%. The individual estimates in the table ranged from Seidel's[3] (3%) to Dana's[4] (17%). This difference is doubtless due in some degree to the personal equation.

This element may be lessened by dividing the autopsied cases into three instead of two classes, namely into the operable, the inoperable, and the doubtful, and limiting the designation operable to those cases in which lasting relief might be expected from the operation. Into the operable cases will fall the primary, accessible, well defined tumors which may be removed without cutting into brain tissue. Such tumors spring, in the great majority of cases, from the dura, many of them being designated endotheliomata, a term including the spindle-celled sarcomata and certain psammomata, growths in which, according to Blackburn,[5] groups or whorls of cells have undergone hyaline degeneration and calcification. The modern tendency seems to be to class these tumors according to the nature of the growth so degenerated, for example, spindle-celled sarcomata, rather than according to the form of degeneration. But into the realm of histological classification we should not venture to penetrate.

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[1] Read at the meeting of the American Neurological Association, June 1, 2 and 3, 1905.

[2] Boston Med. and Surg. Jour., Oct. 5. 12, and 19, 1889.

[3] Verhand. d. Deutch Gessellsh, f. Chir., 1892.

[4] British Med. Jour., Oct. 16, 1897.

Into the inoperable class fall the cases generally so acknowledged, such as tumors involving the deeper structures of the brain, the basal ganglia, the pituitary body or the middle lobe of the cerebellum, gliomata extensively involving and replacing brain tissue, as well as most cases of multiple growths and of widespread metastasis.

In the third, or doubtful class, may be placed gliomata and non-encapsulated sarcomata at or near the surface of the brain in accessible regions, many subtentorial tumors, and cysts in which operation can accomplish nothing beyond evacuation of their fluid contents. The prevailing scepticism among pathologists regarding the operability of gliomata seems well founded. Such tumors involve a tendency to faulty growth inherent in the brain substance itself, a tendency to which no boundary can be set, and which can no more be checked than the tendency of fruit to decay after removing the portion obviously decayed, a comparison already rather too favorable for the brain because the difficulty in determining the extent of brain destruction in case of a glioma by exploratory operation is, as a rule, much greater than that of determining the limit of decay in the fruit.

With this classification in view, we have gone through the autopsy records, or studied the specimens, or both, in 221 cases. These cases, with the exception of 15 taken from our own private records, were kindly placed at our disposal for this purpose by the pathologists of the Massachusetts General Hospital, the Boston City Hospital, the Danvers, the Taunton and the Worcester Insane Hospitals, the New York City Hospital, the Montefiore Home, and the Mt. Sinai Hospital of New York City, by the Curator of the Warren Museum, by Dr. Harlow Brooks of New York, and Dr. J. J. Putnam and Dr. E. W.

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[5] "Intercranial Tumors Among the Insane," 1902. Washington. Government Printing Office.

Taylor from their private collections, and by Dr. Knapp from his recent collection which includes the remainder of the Boston City Hospital cases. The published reports of autopsies found in *Brain* since the establishment of that journal in Blackburn's recent report, and in Knapp's[6] collection of 1891, have been included to bring the total number to 424, a sufficiently large number of consecutive observations to lessen, as far as possible, any selective tendency in the collection. The result of this study is as follows: Out of 424 cases 30, or 7%, were operable; 338, or 80%, were inoperable, and 56, or 13%, were placed in the doubtful class. The combination of operable and possibly operable therefore reached 20%.

Eliminating, on the other hand, the cases in which metastasis or infection was elsewhere present and the cases in which it was stated that no diagnostic symptoms were present, the number of operable cases was reduced to 14, or 3.3%, the doubtful to 34, or 8%. This analysis shows that the highest proportion of operable cases noted in previous statistics (17%) may be approximated in our cases by including the doubtful or possibly operable among the operable, and that, on the other hand, the lowest estimate (3%) may be approximated by including only the undoubtedly operable and excluding those without distinctive symptoms and those with infection elsewhere.

The percentage of possibly operable cases could have been materially increased by accepting the liberal construction of Mills,[7] who cites as probably operable Preston's cerebellar tumor, described as a bilobar tumor, compressing the vermis like a saddle in its inferior part, also exerting some compression upon the quadrigeminum, and apparently having attachments to the callosum, falx and tentorium.

A number of operable growths failed to show localizing symptoms. Many of these were growths near the median line and under the frontal or temporo-sphenoidal lobes rather than in the regions of the convexity usually explored. These facts should lead us to advise exploration over the surface of the brain, particularly in these directions, in preference to following the common method of puncturing the brain substance in various directions in search of a deeply lying tumor. The reason for the continued futility of the latter procedure becomes evident upon the study of a series of autopsies, in which the absence of deep encapsulated tumors is noteworthy. The possibility of the evacuation of a cyst by puncture is of course always present, but this seems the only hope that justifies the procedure, and the hope of permanent relief by such evacuation is small compared with that of finding, for example, an endothelioma by extended search over the surface of the brain. If it should seem advisable and safe to follow both plans in a given case, the surface exploration should certainly precede the tapping.

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[6] "Intercranial Growths." Boston, 1891.

[7] New York Med. Jour., Feb. 11, 1905.

The method of exploration here suggested would probably have changed an unsuccessful to a successful operation in at least one of the cases included in this study, in which an easily removeable endothelioma was found on autopsy, somewhat nearer the median line, in the parietal region, than the site of operation.

It is interesting to note the comparatively simple pathological classification of brain tumors in recent times. Whereas in the early table of Bernhardt[8] 25 distinct varieties of tumor were mentioned, at present nearly all are included under the essential growths of the nervous system (glioma), the connective tissue or non-epthelial growths (fibroma, sarcoma, endothelioma, angioma, angio-sarcoma, osteoma), the epithelial (carcinoma, cholesteatoma), the infectious granulomata (tubercle, gumma and actinomycocis) and the parasitic cysts.

It is interesting to note the infrequency of the diagnosis gumma in recent reports. In fact, this diagnosis does not appear at all in the series of Blackburn, nor does it appear in the Massachusetts General Hospital records since 1896. Multiple tumors of other nature are, however, not uncommon.

These observations are in marked contrast to the frequency with which the clinical diagnosis gumma is made, particularly in case of multiple symptoms. The bearing of this point upon the question under consideration is that the clinical diagnosis gumma should not deter us from advising operation in case of intracranial growth.

Another practical point has been emphasized by this study, namely, the importance of following a fixed plan of operation in spite of previous failures. Two successive autopsy records were found in one hospital in which the symptoms were practically identical and included Jacksonian attacks commencing in the face. Operation in the lower Rolandic region was unsuccessfully undertaken in the first case and not attempted in the second. Operation in the second case in the same region could hardly have failed to disclose and remove, with every prospect of complete recovery, an endothelioma springing from the dura.

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[8] "Beitrage Zur Symptomalogie und Diagnostik der Hirngeschwulste," 1881.

Certain clinical features of cerebral tumor have impressed themselves upon us in this study.

Convulsions.—The clinical records, though often meager, are sufficient to corroborate the fact already established (Knapp, Starr, Mills *et al*) that convulsions in themselves afford little or no help in locating the tumor, as well as the recent dictum of Collier[9] that convulsion, even of the Jacksonian type, is to be discarded as a localizing sign when appearing long after the general signs of intracranial growth. Convulsions accompanied tumors in every situation. The frequency is as follows: frontal 24, cerebellar 15, central convolutions 10, temporo-sphenoidal 11, multiple 7, parietal 6, corpus callosum 5, occipital 4, temporo-parietal 4, pituitary body 3, optic thalamus 2, pineal gland 2, optico-striate 2, centrum ovale 2, temporo-occipital 1, operculum 1, 3d ventricle 1, corpus striatum 2, corpus quadrigeminum 1, lenticular nucleus 1, gyrus fornicatus 1, pons 1.

The frequency of convulsions recorded in cerebellar tumor is of interest in connection with Dana's recent communication. Dana[10] regards sudden fall to one side with loss of sight and consciousness preceded by tinnitus and perhaps accompanied by brief tonic spasm, pathognomic of cerebellar tumor, particularly tumor occupying the cerebello-pontile angle.

Headache and Vomiting.—We have found record of headache together with vomiting in 91 cases, of headache without record of vomiting in 65, of vomiting without record of headache in 11 only.

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[9] "The False Localizing Signs of Intracranial Tumors." Brain, Winter 1904, p. 490.

[10] New York Med. Jour., Feb. 11, 1905.

Mental symptoms.—We find mental symptoms in 97 records without including the cases taken from insane hospitals, in some of which, also, the mental symptoms were doubtless due solely to the tumor. The symptoms noted are as follows: loss of memory, stupor, flippancy, delusions of suspicion and of persecution, anxious condition, excitement, dementia, disorientation, abusiveness, viciousness, apprehension, irritability, incoherence, loss of attention, dulness, apathy, forgetfulness, hysterical manifestations, emotional states, hebetude, confusion, amorousness, oddness, fatuousness, lethargy, depression, vacuity, volubility, euphoria, indefference, silliness, delirium, childishness and simple mental failure. It must be remembered that tumor is not necessarily excluded in dementia because of the absence of cardinal tumor symptoms.

Pupils.—Every variety of pupillary disturbance appeared, most commonly sluggishness of reaction. It would seem that little asistance in localization is to be expected from this quarter.

Reflexes.—There is need for an enormous amount of detailed labor before an exact idea can be reached of the location of the mechanisms concerned in the various reflexes and their inter-relations.

The only attempt we shall now make is to add to the existing series of cases showing an appreciable per cent. of diminished reflexes in brain tumor, and to indicate the direction in which this investigation should be pursued,—namely, toward discovering what cerebral lesions cause lessened, and what cause increased, reflexes; and why lesions in some locations cause lessening of reflexes at one period and increase at another. It is noteworthy that the evidence of these cases tends to strengthen the views of those who regard the brain not simply as inhibitive but as playing an active (and in health the principal) part in the production of the so-called reflex phenomena.

In the 123 cases in which record of reflexes was found the knee-jerks were noted simply as *increased* in the following: frontal 8, corpus callosum 5, occipital 4, pituitary body 4, temporo-sphenoidal 3, centrum ovale 3, caudate nucleus 1, cerebellar 3, parietal 2, central convolutions 2, quadrigemini, pons and medulla, multiple, and not stated, each 1, making a total of 39.

The knee-jerks were noted simply as *diminished or absent* in the following: frontal 7, cerebellar 5, pituitary body 4, corpus callosum 3, temporo-sphenoidal 2, occipital, pons, thalamus, centrum ovale, quadrigeminal, and multiple, each 1, making a total of 27. [illegible] case the knee-jerk on the opposite side was at first increased.

The knee-jerk was *increased on the side opposite the tumor* in the following: tumors of central convolutions 5, corpus callosum 4, parietal, cerebellum, pons and medulla, and multiple, each 1, making a total of 13. It was increased in the early history in the thalamus case mentioned above.

The knee-jerk was *increased on the side of the tumor* in one case (thalamus).

The knee-jerk was *decreased on the paralyzed side* in the following: frontal 2, occipital, temporo-sphenoidal and pituitary, each 1, making a total of 5.

The superficial reflexes were noted simply as lessened in 5, cases. The knee-jerks were normal in 50 cases.

The superficial reflexes were noted simply as lessened in 5, *lessened on the paralyzed side* in 7, unequal without further specification in 1, normal in 9.

Lessening of deep reflexes was recorded then in 31 out of 135 cases; increase in 53.

Lessening of superficial reflexes was recorded in 12 out of 21 cases, or more than half.

It is to be hoped that as a matter of routine more complete hospital records will be made in the future than have been made in the past, in order that the value of such records for statistical purposes may be increased.

Even the meagre findings here noted suggest that it is worth while to carry on the study of the brain as an important integral part of the reflex mechanism. The lessening of superficial reflexes in more than half the cases in which these reflexes were noted, certainly tends to bear out the supposition of Grasset that in man the controlling center for these reflexes has risen to the cortex, for if this is true the tendency of all central lesions at whatever height should be to lessen, if affecting them at all. Following Grasset's[11] supposition that the controlling mechanism of the deep reflexes has ascended only to the region of the basal ganglia (particularly the red nucleus, van Gehuchten's tendon-reflex center) there should be, as we have found, great variation in the deep reflexes in cerebral tumors, but including less cases of lost knee-jerk (about 25%) than of increased knee-jerk (about 41%), since the chance of total destruction of the reflex arcs is less than that of interfering with the inhibiting mechanism, which is presumably at a higher level, and perhaps more extensive.

In certain cases of tumor limited to the cortex, the deep reflexes were exaggerated while all the superficial reflexes (unless the Babinski be so classed) were diminished or lost on the paralyzed side and normal on the other. Such cases tend to fortify Grasset's supposition

It is also of interest in connection with this theory to note the proportion of diminished to increased knee-jerks in the central and parietal convolutions, the centrum ovale, and the corpus callosum, as contrasted with that in and below the basal ganglia (corpora quadrigemina, pons and medulla) as well as in the cerebellum.

Classified in this way we find:—

In central convolution tumors the knee-jerk was increased in 7 cases, decreased in none; parietal increased in 3, diminished in none; centrum ovale, increased in 3, diminished in one; corpus callosum, increased in 9, diminished in 3.

Among tumors of the basal ganglia, corpus quadrigeminum, pons and medulla, the knee-jerk was increased in 5, diminished in 3 (in one case of thalamus tumor the knee-jerk was increased only in the early stages).

Among cerebellar tumors the knee-jerk was increased in 4, diminished in 5 cases.

Of tumors in other localities we find frontal 8 increased, 9 decreased; temporo-sphenoidal, 3 increased, 3 decreased; pituitary body, 4 increased, 5 decreased; occipital, 4 increased, 2 decreased.

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[11] Grasset. "Les maladies de l'orientation et de l'equilibre," Paris, 1901, p. 74. See also Revue Neurologique, 1900, p. 737.

Among recent reports Raymond[12] cites a sarcoma pressing on the right peduncle and neighboring corpus quadrigeminum with absence of reflexes of the lower extremities. He regards the phenomenon due not to posterior column degeneration, but to compression of the medulla by stasis of the cerebrospinal fluid. He calls attention to the absence of other symptoms of posterior column disease in case of cerebral tumor, and reminds us that this degeneration was a purely anatomical discovery.

It is of interest in this connection to note that Reh[13] has studied the clinical histories of 100 cases in the literature with reference to the question of lessened and lost knee-jerks in cerebral disease, and the relation of this sign to posterior column degeneration. He explains the diminished reflexes in most cases by the posterior column degeneration (which he does not regard as due to posterior root injury). He explains the fact that the knee-jerk is often normal or increased in spite of this degeneration by variation in seat and degree of the degeneration. Certain cases of varying reflex he attributes to variation of pressure. This is in line with the explanations generally accepted; Batten and Collier,[14] for example, attribute lost knee-jerk in cerebral tumor to posterior column degeneration, but add that if the knee-jerk is normal this does not eliminate posterior column degeneration.

All such explanations start with the assumption that loss of knee-jerk can only be produced by damage to the spinal segments. But is this hypothesis still tenable? The collected observations, clinical, pathological and experimental, seem to point rather to the conclusion that the human mechanisms through which the knee-jerk, for example, is produced, are not simple, and that while the spinal segments in man retain the power to produce the active reflex characteristic of the lower animals, these reflexes in the healthy man are of a different type and represent the composite result of the activity of the spinal paths combined with that of higher paths with which they are in intimate connection. These higher paths are probably in health the controlling part of the mechanism producing the comparatively subdued phenomenon as it appears in the healthy man. To this level may be applied for convenience the term reflex center, provided we recognize the inadequacy of this term in such connection.

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[12] Archive de Neurol., Jan., 1904.

[13] Monat. f. Psych. u. Neurol. Marz, 1904.

[14] "Spinal Cord Changes in Cases of Cerebral Tumor." Brain, 1899, Part 4, p. 473.

It is true that gradual destruction of the higher paths in this mechanism results in exaggerated knee-jerk, a fact which for a long time was deemed adequate to show that the function of the higher path was simply inhibitive; but such destruction does not always produce exaggerated knee-jerk; on the contrary it sometimes results, especially if the destruction is rapid and complete, in a loss of knee-jerk, apparently not always to be explained by the co-existence of spinal lesion.

It is certainly difficult to explain by posterior column degeneration, or spinal trouble, the cases in which the reflex is lessened on the paralyzed side only, that is the side opposite the tumor, to say nothing of the not infrequent temporary loss of knee-jerk on the paralyzed side in the early history of cerebral hemorrhage.

It is true that one case of Finkelnburg, quoted by Reh, suggests that increased pressure of cerebro-spinal fluid may lessen the reflexes. This was the case in which the reflexes, previously absent, returned and became active immediately after lumbar puncture. But even here why should we assume that it was necessarily relief of *spinal*, rather than *cerebral*, pressure that caused the return of the reflexes? But we are not in possession of sufficient data to venture far into the realms of hypothesis. The fact is, however, established that the knee jerk not infrequently disappears in brain tumor, and while confessing our inability to critically analyze all the findings here recorded we submit that they are not easily reconcilable with any theory which accepts the spine as the sole seat of the reflex arcs.

The facts here collected are presented merely as suggestive not as demonstrative or as representing final results. The main object in this branch of the communication is to direct attention to the importance of more complete and careful observations of the locations, and the periods, in which central growths affect the reflexes with a view to furthering the final analysis of the cerebral reflex mechanism.